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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,825	09/22/2000	Satoshi Mori	55022	1169

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EXAMINER
SCHMIDT, MARY M

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/22/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/646,825	Applicant(s) MORI ET AL.	
	Examiner Mary Schmidt	Art Unit 1635	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 22-29* is/are pending in the application.

4a) Of the above claim(s) *1-16* is/are withdrawn from consideration.

5)☒ Claim(s) *25 and 29* is/are allowed.

6)☒ Claim(s) *22-24 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Please note that the Examiner of Record has changed in the instant Application. Please address all future correspondence to Examiner Schmidt. For information on how to contact the Examiner, Applicant is referred to the concluding remarks below.

Election/Restriction

2. Applicant's election of Group II in Paper No. 8, mailed 11/23/01, in a telephonic election is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse since no remarks were filed in the response entered 3/5/02.

4. This application contains claims 1-16 drawn to an invention nonelected with traverse in Paper No. 8, mailed 11/23/01. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 22-24 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claims 22-24 are drawn to a nucleic acid having a modified base sequence which can be used for transforming a useful plant; wherein the region of a factor relating to the poly (A) addition of the mRNA of the useful plant to be transformed contained in the base sequence of the gene of the other species is modified into another base sequence not relating to the poly (A) addition of the mRNA without substantially altering the function of the protein encoded by the gene to be introduced; wherein the nucleic acid is DNA; wherein the gene is DNA is encoding ferric-chelate reductase FRE1.

New claims 26-28 are drawn to a nucleic acid having a modified base sequence for transforming a useful plant, wherein the gene of another species: does not contain a sequence with continued 8 bases or more consisting of only G or T; and, does not contain any of base sequences represented by a sequence NATAAA, ANTAAA, AANAAA, AATNAA, AATANA, or AATAAN in the downstream of GT-rich sequence in the base sequence of the gene of the other species, wherein, when introduced into a useful plant, the gene does not substantially alter the function of the protein encoded by the gene to be introduced; wherein the nucleic acid is DNA; wherein the gene is DNA encoding ferric-chelate reductase FRE1.

MPEP 2163 teaches the following conditions for the analysis of the claimed invention at the time the invention was made in view of the teachings of the specification and level of skill in the art at the time the invention was made:

> **The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence....A lack of written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process....Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement....The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.**

The specification as filed teaches the novel modified FRE1 sequence of SEQ ID NO:1 from *Saccharomyces cerevisiae*. The modified FRE1 was shown to have ferric-chelate reductase activity as shown in instant Figures 16 and 17.

The instant claims are drawn to any modified nucleic acid sequence as reiterated above. The specification describes on page 5 that an "[e]xample of the region of a factor relating to the poly(A) addition of the mRNA is preferably AATAAA like base sequence, further the said

region of a factor relating to the poly(A) addition of the mRNA is preferably the region existing downstream of the GT-rich base sequence." The specification teaches by way of example modification of the yeast FRE1 gene since the full length mRNA of yeast FRE1 introduced into tobacco plants was not able to be expressed due to "addition of poly (A) within the coding region of FRE1." (See page 10 of the specification)

The claims as written encompass any possible nucleic acid gene sequence having any such modification of a downstream area of a GT-rich region by replacing any "region of a factor relating to the poly(A) addition of the mRNA." The nucleic acids are further claimed as functional for use in transforming any plant.

It was not clear at the time the invention was made that Applicant was in possession of a representative number of species of any modified nucleic acid sequence as broadly claimed. The breath of any nucleic acid claimed rests on negative limitations so that Applicants' claim any nucleic acid sequence which potentially has the described "region of a factor relating to the poly(A) addition of the mRNA" in any gene presumably from foreign genes not normally expressed in plants and/or not having the specific regions claimed. The specification as filed doesn't provide any other example genes which would require such modification other that the yeast FRE1 gene for expression in tobacco. Therefore, other than a vague teaching to look for GT-rich areas in any such gene, and change the sequence to remove certain sequences, one of skill in the art would not immediately envision on what is otherwise any possible nucleic acid gene sequence as broadly claimed. The art indicates that the structure of nucleic acid sequences,

ie. any gene for instance, is empirically determined and the structural elements of a gene in one species will have different regulatory sequences and different structural elements. There would be an expectation of substantial variation among species encompassed within the scope of the claims because the location of the claimed regions is not readily known absent empirical testing upon use in a plant. The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO:1 do not provide a substantial correlation to any such modification needed or required in any other nucleic acid sequence broadly claimed. One of skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claims.

One of skill in the art was in possession of the sequence of SEQ ID NO:1, the modified nucleic acid sequence of *Saccharomyces cerevisiae* FRE1 gene.

7. Claims 22-24 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, the *Saccharomyces cerevisiae* FRE1 gene , does not reasonably provide enablement for the scope of possible nucleic acid sequences claimed for use in plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As argued above, the scope of possible sequences claimed was not in possession of one skilled in the art at the time the invention was made. Further, one skilled in the art would have to practice undue experimentation to make and use the scope of possible sequences claimed, thus including use of said sequences in plants.

See the description of the claims above and the description of the teachings of the instant specification described above.

The specification as filed teaches making modifications of the yeast FRE1 gene, specifically making instant SEQ ID NO:1, for use in plants. The specifically generally describes modifications of any other nucleic acid, any gene for expression in plants by modifying regions downstream of GT-rich regions so that certain sequences recognized for poly (A) addition are removed. However, it is not clear from making at least one of the claimed modifications to any possible nucleic acids absent further characterization of the expressed protein in plants, that one of skill in the art would be able to use any such nucleic acid sequence having the function of expression in any plant.

The following teaches generally the state of the art for determining the functionality of any expressed protein from knowing only the nucleic acid sequence:

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can

be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39,

especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427). On of skill in the art would necessarily practice trial and error experimentation to generate the a representative number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity in specific target nucleic acid sequences from foreign genes, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations other than negative structural limitations (ie. sequences not have certain 6-mers), undue experimentation would be required of the skilled artisan to make and use the claimed invention.

Allowable Subject Matter

8. SEQ ID NO:1 was found to be free of the prior art.

9. Claims 25 and 29, would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Kay Pinkney*, whose telephone number is (703) 305-3553.

M. M. Schmidt
May 20, 2002

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600